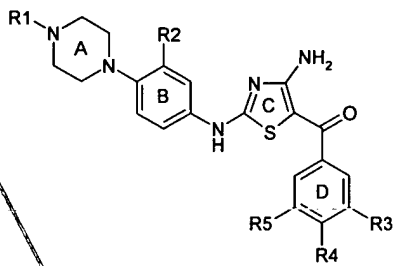


CLAIMS

What is Claimed is:

1. A compound of formula:



or the pharmaceutically acceptable salts or esters thereof, wherein

R¹ is selected from the group consisting of

H,

lower alkyl that optionally may be substituted with a group selected from OR⁶, cycloalkyl, and NR⁷R⁸,

cycloalkyl,

COR⁹, and

SO₂R¹⁰;

R² is selected from the group consisting of

H,

F,

Cl, and

CH₃;

of

R^3 , R^4 and R^5 are each independently selected from the group consisting

H,

lower alkyl, which optionally may be substituted with a group selected from OR^6 and NR^7R^8 ,

OR^{11} ,

$NR^{12}R^{13}$,

halogen,

NO_2 ,

$CONR^6R^9$,

$NHSO_2R^{14}$,

CN

S-lower alkyl,

OCF_3 , and

$OCHF_2$,

or alternatively, R^3 and R^4 taken together with the two carbons and the bond between them from the benzene ring (D) to which R^3 and R^4 are attached can form a ring system having up to two additional rings, each of said rings having 5-7 atoms, and the ring attached to the benzene ring (D) optionally including one or more hetero atoms and being optionally substituted by lower alkyl,

provided that R^3 and R^4 are not simultaneously $-OCH_3$, and provided further that R^4 is not $-Cl$ when R^3 is $-NO_2$;

R^6 and R^9 are independently selected from the group consisting of

H, and

lower alkyl that optionally may be substituted by OH and halogen;

R^7 and R^8 are independently selected from the group consisting of

H, and

lower alkyl that optionally may be substituted by OR^6 ,

or, alternatively, R^7 is H and R^8 is OH,

or, alternatively, NR^7R^8 can optionally form a ring having 5-6 atoms, said ring optionally including one or more additional hetero atoms and being optionally substituted by the group consisting of one or more of OR^6 and lower alkyl which itself may be optionally substituted by OH;

R^{10} is selected from the group consisting of

lower alkyl which optionally may be substituted by one or more chlorine or fluorine, and

NH_2 ;

R^{11} is selected from the group consisting of

H, and

lower alkyl that optionally may be substituted by OR^6 , COOH , halogen and $\text{NR}^{15}\text{R}^{16}$;

R^{12} and R^{13} are independently selected from the group consisting of

H,

lower alkyl that optionally may be substituted with a group selected from OR^6 , COOH and $\text{NR}^{15}\text{R}^{16}$,

COR^{17} , and

SO_2R^{18} ,

provided that only one of R^{12} and R^{13} is COR^{17} or SO_2R^{18} ,

or alternatively $\text{NR}^{12}\text{R}^{13}$ can optionally form a ring having 5-6 atoms, said ring optionally including one or more additional hetero atoms and being optionally

substituted by the group consisting of one or more of OR^6 and lower alkyl which itself may be optionally substituted by OH;

Q3
CH
 R^{14} is lower alkyl;

R^{15} and R^{16} are independently selected from the group consisting of H, and lower alkyl that optionally may be substituted by OH,

or alternatively $\text{NR}^{15}\text{R}^{16}$ can optionally form a ring having 5-6 atoms, said ring optionally including one or more additional hetero atoms and being optionally substituted by the group consisting of one or more of OR^6 and lower alkyl which itself may be optionally substituted by OH;

R^{17} is selected from the group consisting of

H, and

lower alkyl which optionally may be substituted with a group selected from OH, COOH and $\text{NR}^{15}\text{R}^{16}$; and

R^{18} is lower alkyl.

2. The compound of claim 1 wherein R^1 is selected from the group consisting of H, $\text{CH}_2\text{CH}_2\text{OH}$, $\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$, $\text{CH}_3\text{CO}-$, $\text{CH}(\text{CH}_3)_2$, $\text{CH}_2\text{CH}(\text{CH}_3)_2$, cyclopropylmethyl and CH_3 .

3. The compound of claim 2 wherein R^1 is selected from the group consisting of H, methyl, $\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ and $\text{CH}(\text{CH}_3)_2$.

4. The compound of claim 1 wherein R^2 is selected from the group consisting of H and fluorine.

5. The compound of claim 4 wherein R^2 is H.

6. The compound of claim 2 wherein R^2 is selected from the group consisting of H and fluorine.

7. The compound of claim 3 wherein R^2 is H.

8. The compound of claim 1 wherein R^3 is selected from the group consisting of OR^{11} , lower alkyl, NH_2 , Cl, F, H, $OCHF_2$ and NO_2 .

9. The compound claim 6 wherein R^3 is selected from the group consisting of OR^{11} , lower alkyl, NH_2 , Cl, F, H, $OCHF_2$ and NO_2 .

10. The compound of claim 7 wherein R^3 is selected from the group consisting of F, OCH_3 and CH_2CH_3 .

11. The compound of claim 8 wherein R^3 is selected from the group consisting of F, OCH_3 and CH_2CH_3 .

12. The compound of claim 1 wherein R^4 is selected from the group consisting of acetamido, chloro, diethylamino, hydrogen, hydroxy, hydroxyethylamino, [1-(hydroxymethyl)-3-methylbutyl]amino, 1-(3-hydroxymethyl)piperidiny, 4-hydroxy-1-piperidiny, methoxy, 2-methoxyethylamino, 2-methyl-1-pyrrolidiny, morpholino, piperidiny, pyrrolidiny.

13. The compound of claim 12 wherein R^4 is selected from the group consisting of H and CH_3O- .

14. The compound of claim 9 wherein R^4 is selected from the group consisting of acetamido, chloro, diethylamino, hydrogen, hydroxy, hydroxyethylamino, [1-(hydroxymethyl)-3-methylbutyl]amino, 1-(3-hydroxymethyl)

Q3
cont

piperidinyl, 4-hydroxy-1-piperidinyl, methoxy, 2-methoxyethylamino, 2-methyl-1-pyrrolidinyl, morpholino, piperidinyl and pyrrolidinyl.

15. The compound of claim 10, wherein R^4 is selected from the group consisting of acetamido, chloro, diethylamino, hydrogen, hydroxy, hydroxy-ethylamino, [1-(hydroxymethyl)-3-methylbutyl]amino, 1-(3-hydroxymethyl) piperidinyl, 4-hydroxy-1-piperidinyl, methoxy, 2-methoxyethylamino, 2-methyl-1-pyrrolidinyl, morpholino, piperidinyl and pyrrolidinyl.

27. 16. The compound of claim 11, selected from the group consisting of acetamido, chloro, diethylamino, hydrogen, hydroxy, hydroxy-ethylamino, [1-(hydroxymethyl)-3-methylbutyl]amino, 1-(3-hydroxymethyl) piperidinyl, 4-hydroxy-1-piperidinyl, methoxy, 2-methoxyethylamino, 2-methyl-1-pyrrolidinyl, morpholino, piperidinyl and pyrrolidinyl.

17. The compound of claim 1 wherein R^3 and R^4 taken together with the benzene ring to which they are attached form a polycyclic ring system.

18. The compound of claim 17 wherein the ring system is selected from the group consisting of 2-dibenzofuranyl, 1,3-benzodioxol-5-yl, 2,3-dihydro-1,4-benzodioxin-6-yl, and 3,4-dihydro-2H-1,5-benzodioxepin-7-yl.

19. The compound of claim 6 wherein R^3 and R^4 taken together with the benzene ring to which they are attached form a polycyclic ring system.

20. The compound of claim 7 wherein R^3 and R^4 taken together with the benzene ring to which they are attached form a polycyclic ring system.

Q3
cont

21. The compound of claim 19 wherein the ring system selected from the group consisting of 2-dibenzofuranyl, 1,3-benzodioxol-5-yl, 2,3-dihydro-1,4-benzodioxin-6-yl, or 3,4-dihydro-2H-1,5-benzodioxepin-7-yl.

22. The compound of claim 20 wherein the ring system selected from the group consisting of 2-dibenzofuranyl, 1,3-benzodioxol-5-yl, 2,3-dihydro-1,4-benzodioxin-6-yl, or 3,4-dihydro-2H-1,5-benzodioxepin-7-yl.

23. The compound of claim 17 which is selected from the group consisting of:

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](2,3-dihydro-1,4-benzodioxin-6-yl)methanone,

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](1,3-benzodioxol-5-yl)methanone,

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](3,4-dihydro-2H-1,5-benzodioxepin-7-yl)methanone,

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](2-dibenzofuranyl)methanone,

[4-Amino-2-[[3-fluoro-4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](1,3-benzodioxol-5-yl)methanone,

[4-Amino-2-[[4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-5-thiazolyl](2,3-dihydro-1,4-benzodioxin-6-yl)methanone,

[4-Amino-2-[[4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-5-thiazolyl](1,3-benzodioxol-5-yl)methanone,

1-Acetyl-4-[4-[[4-amino-5-[(1,3-benzodioxol-5-yl)carbonyl]-2-thiazolyl]amino]phenyl]piperazine, and

[4-Amino-2-[[4-[4-(2-hydroxyethyl)-1-piperazinyl]phenyl]amino]-5-thiazolyl](2,3-dihydro-1,4-benzodioxin-6-yl)methanone.

24. The compound of claim 17 which is selected from the group consisting of:

[4-Amino-2-[[3-fluoro-4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](2,3-dihydro-1,4-benzodioxin-5-yl)methanone,

(4-Amino-2-{4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-phenylamino}-thiazol-5-yl)-benzo[1,3]dioxol-5-yl-methanone,

4-Amino-2-{4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-phenylamino}-thiazol-5-yl)-(2,3-dihydro-benzo[1,4]dioxin-6-yl)-methanone,

{4-Amino-2-[4-(4-sec-butyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-benzo[1,3]dioxol-5-yl-methanone,

{4-Amino-2-[4-(4-sec-butyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(2,3-dihydro-benzo[1,4]dioxin-6-yl)-methanone,

{4-Amino-2-[4-(4-cyclopentyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-benzo[1,3]dioxol-5-yl-methanone,

{4-Amino-2-[4-(4-cyclopentyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(2,3-dihydro-benzo[1,4]dioxin-6-yl)-methanone,

~~{4-Amino-2-[4-(4-cyclopropylmethyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-benzo[1,3]dioxol-5-yl-methanone, and~~

~~{4-Amino-2-[4-(4-cyclopropylmethyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(2,3-dihydro-benzo[1,4]dioxin-6-yl)-methanone.~~

25. The compound of claim 1 wherein R⁵ is selected from the group consisting of H and F.

26. The compound of claim 25 wherein R⁵ is F.

27. The compound of claim 19 wherein R⁵ is F.

28. The compound of claim 22 wherein R⁵ is F.

29. The compound of claim 26 which is selected from the group consisting of:

[4-Amino-2-[[4-[4-(2-hydroxyethyl)-1-piperazinyl]phenyl]amino]-5-thiazolyl] (3,5-difluorophenyl)methanone,

{4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3,5-difluoro-phenyl)-methanone,

(4-Amino-2-{4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-phenylamino}-thiazol-5-yl)-(3,5-difluoro-phenyl)-methanone,

{4-Amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3,5-difluoro-phenyl)-methanone, and

~~[4-Amino-2-(4-piperazin-1-yl-phenylamino)-thiazol-5-yl]-(3,4,5-trifluorophenyl)-methanone.~~

30. The compound of claim 25 wherein R⁵ is H.

31. The compound of claim 1 wherein at least one of R³, R⁴ and R⁵ is halogen.

32. The compound of claim 31 which is selected from the group consisting of:

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](3,4-dichlorophenyl)methanone,

[4-Amino-2-[[4-[4-(2-hydroxyethyl)-1-piperazinyl]phenyl]amino]-5-thiazolyl](3-fluorophenyl)methanone,

[4-Amino-2-[[4-(1-piperazinyl)phenyl]amino]-5-thiazolyl](3-fluorophenyl)methanone,

{4-Amino-2-[4-[4-(3-hydroxy-propyl)-piperazin-1-yl]-phenylamino]-thiazol-5-yl}-(3-fluoro-phenyl)-methanone,

{4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3-fluoro-phenyl)-methanone,

{4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3,4,5-trifluoro-phenyl)-methanone,

Q3
Chemist
(4-Amino-2-{4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-phenylamino}-thiazol-5-yl)-(3,4-difluoro-phenyl)-methanone,

(4-Amino-2-{4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-phenylamino}-thiazol-5-yl)-(3-fluoro-phenyl)-methanone,

{4-Amino-2-[4-(4-sec-butyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3-fluoro-phenyl)-methanone,

{4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3-fluoro-phenyl)-methanone, and

{4-Amino-2-[4-(4-cyclopropylmethyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3-fluoro-phenyl)-methanone.

33. The compound of claim 1 wherein at least one of R³, R⁴ and R⁵ is selected from the group consisting of OR¹¹, OCF₃, and OCHF₂.

34. The compound of claim 33 which is selected from the group consisting of:

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl]-(4-hydroxyphenyl)methanone,

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](4-methoxyphenyl)methanone,

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](3-fluoro-4-methoxyphenyl)methanone,

Ant
[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](3-methoxyphenyl)methanone,

[4-Amino-2-[[3-fluoro-4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](3,5-dimethoxyphenyl)methanone,

[4-Amino-2-[[3-fluoro-4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](3-methoxyphenyl)methanone,

[4-Amino-2-[[4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-5-thiazolyl](3-methoxyphenyl)methanone,

[4-Amino-2-[[4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-5-thiazolyl](3,5-dimethoxyphenyl)methanone,

[4-Amino-2-[[4-[4-(2-hydroxyethyl)-1-piperazinyl]phenyl]amino]-5-thiazolyl](3-methoxyphenyl)methanone, and

[4-Amino-2-[[4-(1-piperazinyl)phenyl]amino]-5-thiazolyl](3-fluoro-4-methoxyphenyl)methanone.

35. The compound of claim 33 which is selected from the group consisting of:

{4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3-methoxy-phenyl)-methanone,

(4-Amino-2-{4-[4-(3-hydroxy-propyl)-piperazin-1-yl]-phenylamino}-thiazol-5-yl)-(3-methoxy-phenyl)-methanone,

Q3
cont

4-Amino-2-{4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-phenylamino}-thiazol-5-yl)-(3-fluoro-4-methoxy-phenyl)-methanone,

{4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(4-fluoro-3-methoxy-phenyl)-methanone,

{4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3-fluoro-4-methoxy-phenyl)-methanone,

{4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(4-difluoromethoxy-phenyl)-methanone,

{4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3-trifluoromethoxy-phenyl)-methanone,

(4-Amino-2-{4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-phenylamino}-thiazol-5-yl)-(3-methoxy-phenyl)-methanone,

{4-Amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3,5-difluoro-4-methoxy-phenyl)-methanone, and

{4-Amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(4-fluoro-3-methoxy-phenyl)-methanone.

36. The compound of claim 33 which is selected from the group consisting of:

{4-Amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3-trifluoromethoxy-phenyl)-methanone,

Q³
cont

[4-Amino-2-(4-piperazin-1-yl-phenylamino)-thiazol-5-yl]-(3,5-difluoro-4-methoxy-phenyl)-methanone,

[4-Amino-2-(4-piperazin-1-yl-phenylamino)-thiazol-5-yl]-(4-fluoro-3-methoxy-phenyl)-methanone,

[4-Amino-2-(4-piperazin-1-yl-phenylamino)-thiazol-5-yl]-(3-trifluoromethoxy-phenyl)-methanone,

[4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl]-(3-trifluoromethoxy-phenyl)-methanone,

[4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl]-(3-difluoromethoxy-phenyl)-methanone,

[4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl]-(3-hydroxy-phenyl)-methanone,

[4-Amino-2-[4-(4-isobutyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl]-(3-hydroxy-phenyl)-methanone,

[4-Amino-2-(4-piperazin-1-yl-phenylamino)-thiazol-5-yl]-(3-difluoromethoxy-phenyl)-methanone,

[4-Amino-2-[4-(4-cyclopropylmethyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl]-(3-difluoromethoxy-phenyl)-methanone,

[4-Amino-2-[4-(4-cyclopropylmethyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl]-(3-methoxy-phenyl)-methanone,

10042619-010902

Q3
cont

~~{4-Amino-2-[4-(4-cyclopropylmethyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3-fluoro-4-hydroxy-phenyl)-methanone,~~

~~{4-Amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3-difluoromethoxy-phenyl)-methanone,~~

~~{4-Amino-2-[4-(4-cyclopropylmethyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3-fluoro-4-methoxy-phenyl)-methanone, and~~

~~{4-Amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(3-hydroxy-phenyl)-methanone~~

37. The compound of claim 1 wherein each of R³, R⁴ and R⁵ is independently selected from NO₂, NHSO₂R⁴ and NR¹²R¹³.

38. The compound of claim 37 which is selected from the group consisting of:

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl][4-(1-pyrrolidinyl)phenyl]methanone,

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl][4-(1-piperidinyl)phenyl]methanone,

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl][4-(4-morpholinyl)phenyl]methanone, acetate salt,

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](3-nitrophenyl)methanone,

Q3
cont

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl][4-(diethylamino)phenyl]methanone,

N-[4-[[4-Amino-2-[[4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-5-thiazolyl]carbonyl]phenyl]acetamide,

[4-Amino-2-[[4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-5-thiazolyl][4-(diethylamino)phenyl]methanone,

1-Acetyl-4-[4-[[4-amino-5-[4-(diethylamino)benzoyl]-2-thiazolyl]amino]phenyl]piperazine, trifluoroacetate salt,

[4-Amino-2-[[4-[4-(2-hydroxyethyl)-1-piperazinyl]phenyl]amino]-5-thiazolyl][4-(1-pyrrolidiny]phenyl]methanone,

[4-Amino-2-[[4-(1-piperazinyl)phenyl]amino)-5-thiazolyl][4-(1-pyrrolidiny]phenyl]methanone, and

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl][4-(2-hydroxyethyl)amino-3-nitrophenyl]methanone.

39. The compound of claim 37 which is selected from the group consisting of:

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl][3-nitro-4-(1-pyrrolidiny]phenyl]methanone,

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl][3-nitro-4-(4-morpholiny]phenyl]methanone,

A³
cont

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl][3-nitro-4-
[(2-methoxyethyl)amino]phenyl]methanone,

racemic [4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl]
[3-nitro-4-[3-(hydroxymethyl)-1-piperidiny]phenyl]methanone,

racemic [4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl]
[3-nitro-4-(2-methyl-1-pyrrolidiny]phenyl]methanone,

(R)-[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl][3-
nitro-4-[[1-(hydroxymethyl)-3-methylbutyl]amino]phenyl]methanone,

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl][3-nitro-4-
(4-hydroxy-1-piperidiny]phenyl]methanone,

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl][3-amino-
4-(4-pyrrolidiny]phenyl]methanone, and

(R)-[3-Amino-4-[[1-(hydroxymethyl)-3-methylbutyl]amino]phenyl][4-amino-
2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl]methanone.

40. The compound of claim 37 which is selected from the group
consisting of:

[4-Amino-2-[[3-fluoro-4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl]
[4-(1-pyrrolidiny]phenyl]methanone,

(4-Amino-2-{4-[4-(3-hydroxy-propyl)-piperazin-1-yl]-phenylamino}-thiazol-
5-yl)-(3-nitro-phenyl)-methanone,

~~{4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(4-piperidin-1-yl-phenyl)-methanone, and~~

~~{4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-(4-morpholin-4-yl-phenyl)-methanone.~~

41. The compound of claim 1 wherein any one or more of R^3 , R^4 and R^5 is CN.

42. The compound of claim 41 which is selected from the group consisting of:

3-(4-Amino-2-{4-[4-(3-hydroxy-propyl)-piperazin-1-yl]-phenylamino}-thiazole-5-carbonyl)-benzonitrile,

3-{4-Amino-2-[4-(4-isopropyl-piperazin-1-yl)-phenylamino]-thiazole-5-carbonyl}-benzonitrile, and

3-{4-Amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazole-5-carbonyl}-benzonitrile.

43. The compound of claim 1 wherein each one of R^3 , R^4 and R^5 is independently selected from H and lower alkyl.

44. The compound of claim 43 which is selected from the group consisting of:

(4-Amino-2-{4-[4-(3-hydroxy-propyl)-piperazin-1-yl]-phenylamino}-thiazol-5-yl)-m-tolyl-methanone,

(4-Amino-2-{4-[4-(3-hydroxy-propyl)-piperazin-1-yl]-phenylamino}-thiazol-5-yl)-(3-ethyl-phenyl)-methanone,

a³ cont
{4-Amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl)-(3-ethyl-phenyl)-methanone, and

{4-Amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-m-tolyl-methanone.

45. The compound of claim 1 wherein at least one of R³, R⁴ and R⁵ is selected from S-lower alkyl.

46. The compound of claim 45 which is {4-Amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}(3-methylsulfanyl-phenyl)-methanone.

47. A compound selected from the group consisting of:

[4-Amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](2,3-dihydro-1,4-benzodioxin-6-yl)methanone, and

[4-Amino-2-[[4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-5-thiazolyl](3-methoxyphenyl)methanone.

48. The compound 1-(4-isothiocyanatophenyl)-4-(1-methylethyl)piperazine.

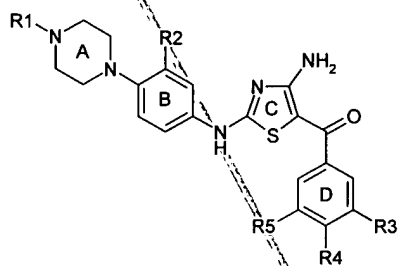
49. The compound 4-(2-hydroxyethyl)-1-(4-isothiocyanatophenyl)piperazine.

50. The compound carbamimidothioic acid, [[4-(4-methyl-1-piperazinyl)phenylamino]thioxomethyl], polymer bound.

51. The compound carbamimidothioic acid, [[4-[4-(1-methylethyl)-1-piperazinyl]phenylamino]thioxomethyl], polymer bound.

52. The compound carbamimidothioic acid, [[4-[4-(2-hydroxyethyl)-1-piperazinyl]phenylamino]thioxomethyl], polymer bound.

53. A compound of formula:



or the pharmaceutically acceptable salts or esters thereof, wherein

R¹ is selected from the group consisting of

H, and

lower alkyl that optionally may be substituted by OR⁶;

R² is selected from the group consisting of H and F;

R³ is selected from the group consisting of

H,

lower alkyl

Q³
cont

halogen,
NR¹²R¹³,
NO₂,
OCHF₂, and
OR¹¹,

R⁴ is selected from the group consisting of

H,
lower alkyl that optionally may be substituted by OR⁶,
halogen,
NR¹²R¹³,

or alternatively, R³ and R⁴ taken together with the two carbons and the bond between them from the benzene ring (D) to which R³ and R⁴ are attached can form a ring system having up to two additional rings, each of said rings having 5-7 atoms, and the ring attached to the benzene ring (D) optionally including one or more hetero atoms and being optionally substituted by lower alkyl,

provided that R⁴ is not -Cl when R³ is -NO₂;

R⁶ is selected from the group consisting of

H, and
methyl;

R¹¹ is selected from the group consisting of

H, and
lower alkyl that optionally may be substituted by a group selected from OR⁶, COOH, halogen and NR¹⁵R¹⁶;

R¹² and R¹³ are independently selected from the group consisting of

H,

205070-679000

lower alkyl that optionally may be substituted with a group selected from OR^6 , $COOH$ and $NR^{15}R^{16}$,

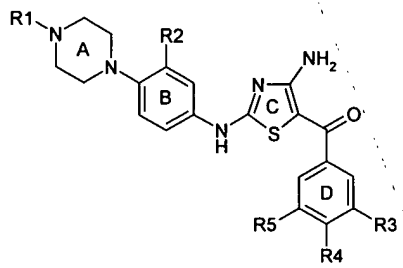
or alternatively $NR^{12}R^{13}$ can optionally form a ring having 5-6 atoms, said ring optionally including one or more additional hetero atoms and being optionally substituted by the group consisting of one or more of OR^6 and lower alkyl which itself may be optionally substituted by OH ; and

R^{15} and R^{16} are independently selected from the group consisting of
H, and

lower alkyl that optionally may be substituted by OH ,

or alternatively $NR^{15}R^{16}$ can optionally form a ring having 5-6 atoms, said ring optionally including one or more additional hetero atoms and being optionally substituted by the group consisting of one or more of OR^6 and lower alkyl which itself may be optionally substituted by OH .

54. A compound of formula:



or the pharmaceutically acceptable salts or esters thereof, wherein

R^1 is selected from the group consisting of

H,

CH_2CH_2OH ,

$CH_2CH_2CH_2OH$,

Q³
cont

CH₃CO-,
CH(CH₃)₂,
CH₂CH(CH₃)₂,
cyclopropylmethyl, and
CH₃;

R² is selected from the group consisting of
H and F;

R³ is selected from the group consisting of
OR¹¹,
lower alkyl,
NH₂,
Cl,
F,
H,
OCHF₂, and
NO₂;

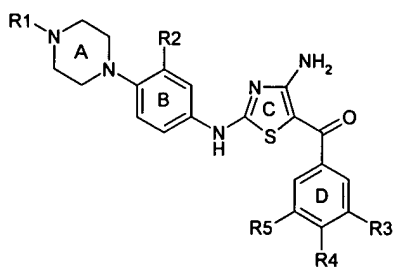
R⁴ is selected from the group consisting of
H, and
diethylamino;

R⁵ is H; and

R¹¹ is unsubstituted lower alkyl.

2105070" 6T32400F

55. A compound of formula:



or the pharmaceutically acceptable salts or esters thereof, wherein

R¹ is selected from the group consisting of

H,
CH₂CH₂CH₂OH,
CH(CH₃)₂,
CH₃, and
cyclopropylmethyl;

R², R⁴ and R⁵ are H; and

R³ is selected from the group consisting of

OCH₃,
F, and
CH₂CH₃.

56. A pharmaceutical composition comprising as an active ingredient an effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier or excipient.

57. The pharmaceutical composition of claim 56 which is suitable for parenteral administration.

58. A method for treating cancer comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to claim 1.

59. The method of claim 58 wherein the cancer is a solid tumor.

60. The method of claim 59 wherein the solid tumor is a breast, colon, lung or prostate tumor.

61. A compound selected from the group consisting of:

1-(2-Fluoro-4-isothiocyanatophenyl)-4-methylpiperazine,
1-(1-Methylethyl)-4-(4-nitrophenyl)piperazine,
4-[4-(1-Methylethyl)-1-piperazinyl]benzenamine,
1-(4-Isouthiocyanatophenyl)-4-(1-methylethyl)piperazine,
4-(2-Hydroxyethyl)-1-(4-isothiocyanatophenyl)piperazine,
1-(4-Isouthiocyanatophenyl)-4-(2-methoxy-ethyl)piperazine,
1-(4-Isouthiocyanatophenyl)-4-(1-methylpropyl)piperazine,
4-Cyclopentyl-1-(4-isothiocyanatophenyl)piperazine,
1-(4-Isouthiocyanatophenyl)-4-(2-methylpropyl)piperazine, and
4-(3-Hydroxypropyl)-1-(4-isothiocyanatophenyl)piperazine.

62. A compound selected from the group consisting of:

2-Bromo-1-(3,4,5-trifluoro-phenyl)ethanone,
2-Bromo-1-(4-fluoro-3-methoxy-phenyl)ethanone,
2-Bromo-1-(4-fluoro-3-methoxy-phenyl)ethanone, and
2-Bromo-1-(3-difluoromethoxy-phenyl)ethanone.

A³
cont

63. A compound selected from the group consisting of:

Carbamimidothioic acid, [[4-(4-methyl-1-piperazinyl)phenylamino]thioxomethyl], polymer bound,

Carbamimidothioic acid, [[3-fluoro-4-(4-methyl-1-piperazinyl)phenylamino]thioxomethyl], polymer bound,

Carbamimidothioic acid, [[4-[4-(1-methylethyl)-1-piperazinyl]phenylamino]thioxomethyl], polymer bound,

Carbamimidothioic acid, [[4-(4-acetyl-1-piperazinyl)phenylamino]thioxomethyl], polymer bound,

Carbamimidothioic acid, [[4-[4-(2-hydroxyethyl)-1-piperazinyl]phenylamino]thioxomethyl], polymer bound,

Carbamimidothioic acid, [[4-[4-[(1,1-dimethylethoxy)carbonyl]-1-piperazinyl]phenylamino]thioxomethyl], polymer bound,

Carbamimidothioic acid, [[4-[4-(2-methoxyethyl)-1-piperazinyl]phenylamino]thioxomethyl], polymer bound,

Carbamimidothioic acid, [[4-[4-(1-methylpropyl)-1-piperazinyl]phenylamino]thioxomethyl], polymer bound,

Carbamimidothioic acid, [[4-(4-cyclopentyl-1-piperazinyl)phenylamino]thioxomethyl], polymer bound,

Carbamimidothioic acid, [[4-[4-(2-methylpropyl)-1-piperazinyl]phenylamino] thioxomethyl], polymer bound, and

Carbamimidothioic acid, [[4-[4-(3-hydroxypropyl)-1-piperazinyl]phenylamino] thioxomethyl], polymer bound.

64. A compound selected from the group consisting of:

[4-amino-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-thiazolyl](4-chloro-3-nitrophenyl)methanone,

4-[4-[[4-Amino-5-(3-fluorobenzoyl)-2-thiazolyl]amino]phenyl]-1-piperazinecarboxylic acid, 1,1-dimethylethyl ester,

4-[4-[[4-Amino-5-[4-(1-pyrrolidiny)benzoyl]-2-thiazolyl]amino]phenyl]-1-piperazinecarboxylic acid, 1,1-dimethylethyl ester, and

4-[4-[[4-Amino-5-(3-fluoro-4-methoxybenzoyl)-2-thiazolyl]amino]phenyl]-1-piperazinecarboxylic acid, 1,1-dimethylethyl ester.

205070 " 6T92400F

a³
cont